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Epidemiology and Prevention

Human recombinant soluble ACE2 (HrsACE2) application and mechanism of action in coronavirus disease 2019

Alireza Pouramini[1*], Fatemeh Kafi[2], Sina Bakhshaei[3], Bina Bakhshaei[4], Rastina Mehrani[5], Kamyab Karimpour[2]

Implication for health policy/practice/research/medical education: A Finding an effective treatment for COVID-19 is essential because of the severe risks it causes to human health. Previous studies have shown that COVID-19 can penetrate cells and initiate its harmful effects on organs via binding to the angiotensin-converting enzyme 2 (ACE2) receptor. According to recent research, the hrsACE2 receptor may form a link with the virus before engaging with the ACE2 receptor on the cell membrane, preventing the subsequent deleterious effects.
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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused a worldwide pandemic by spreading coronavirus disease 2019 (COVID-19) globally, which resulted in extensive mortality, morbidity, and catastrophic economic damages. Accordingly, knowledge of viral pathogenesis has been essential for developing effective treatments. One potential treatment approach is blocking the viral entrance to the cells. Angiotensin-converting-enzyme-2 (ACE2) is a transmembrane protein by which SARS-CoV-2 enters the target cells (1).

Human cells throughout the cardiovascular system, kidneys, lungs, and intestines express ACE2. SARS-CoV-2 has a stronger affinity than SARS-CoV to bind ACE2, which usually causes more severe disease (2). Angiotensin-converting enzyme 2 modulates the mechanism of angiotensin II type 1 receptor (AT1R) and mitochondrial assembly receptor (MasR) by converting angiotensin II to angiotensin 1-7. The mechanism of action of the AT1R causes vasoconstriction, a rise in vascular permeability, the formation of reactive oxygen species, and an increase in transmembrane proteinase ADAM-17 activity. ADAM-17 is produced as a result of tumor necrosis factor-α (TNF-α) and ATR-1 receptor activation, which cleaves the extracellular juxta-membrane region of ACE2. The MAS receptor pathway causes vasodilation, natriuresis, anti-inflammation, and the release of nitric oxide (NO) (3, 4).

A genetically altered version of ACE2 created by Apeiron Biologics is called human recombinant soluble ACE2 (hrsACE2). HrsACE2 stopped the spread of SARS-CoV-2 by binding to the virus' spike protein(3). In cell culture studies, hrsACE2 can reduce SARS-CoV-2 load by a ratio of 1000-5000 (3). Several studies have found that hrsACE2 therapy is effective in COVID-19 patients. hrsACE2 has shown a half-life of 10 hours, which has been shown to be well tolerated in healthy people (5). In a pilot clinical trial, hrsACE2 was given to 10 intensive care unit patients aged 18-80 on mechanical ventilation for less than 72 hours. Subsequently, the level of angiotensin II dropped quickly, without significantly changing their blood pressure. At the same time, the levels of both angiotensin 1-5 and angiotensin 1-7 went up. Furthermore, interleukin-6 concentration, which is important in cytokine storms, exhibited a lower trend than the placebo group (6). Hence, severe cases would get benefit from hrsACE2 treatment by diminishing exaggerated immune response and alleviating its devastating effects.

Initial studies on hrsACE2 have been encouraging, but in some cases, hypotension and acute renal injury are observed due to decreased angiotensin II synthesis. Thus, additional research is required to comprehend better the benefits and adverse effects of hrsACE2 in various clinical settings (7).

Authors' contribution

Conceptualization: AP, FK; Validation: AP; Resources: AP, FK; Data Curation: AP; Writing—Original Draft Preparation: AP; Writing—Review and Editing: SB, BB, RM & KK; Visualization: AP; Supervision: AP, SB; Project Administration: AP.

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[1]Urology Research Center, Tehran University of Medical Sciences, Tehran, Iran. [2]Nickan Research Institute, Isfahan, Iran. [3]Internal Medicine Department, UHS SoCal Medical Education Consortium Temecula, Ca, USA. [4]Neurology Department, Median Klinik NRZ, Wiesbaden, Germany. [5]School of Medicine, St George University, Grenada
***Corresponding author:** Alireza Pouramini, Email: alirezapouraminiarpa@gmail.com

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

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